REMARKS

Entry of the foregoing and prompt and favorable consideration of the subject application, in light of the following remarks, are respectfully requested.

By the present amendment, the specification has been amended in accordance with the amendments made in parent application Serial No. 08/682,794. More specifically, the Abstract has been inserted on a separate sheet after the last page of the claims. Further, the specification has been amended to correct certain grammatical errors which appear to have arisen as a result of the translation of the PCT application from French to English. It is noted with particularly that page 5 of the specification has been amended to delete the "perhaps [sic]" and insert "may be" in place thereof. The term "perhaps" is the translation of the term "peut-être" which appears on page 5, line 19, of the PCT application. However, the term "peut-être" contains a typographical error and should have not included the dash: peut être. The proper translation of the corrected term is "may be." Thus, the present application has been amended to recite " . . . DNA sequence may be composed of . . . ." The remaining amendments to the specification were made to correct minor and obvious typographical and/or grammatical errors. Additionally, by the present amendment, new claims 24-37 have been added. Support for the new claims may be found throughout the originally filed application. No new matter has been added.

In the event that there are any questions relating to this Preliminary Amendment, or to the application in general, it would be appreciated if the Examiner would telephone the undersigned attorney concerning such questions so that prosecution of the application may be expedited.

Respectfully submitted,

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Date: August 27, 2001

Attachment to Preliminary Amendment dated August 27, 2001

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Page 5, Paragraph Beginning at Line 19

The objective of a method according to the invention is to prepare a recombinant viral vector for the transfer of an exogenous DNA sequence to a host cell and its expression therein. "Exogenous DNA sequence" is understood to mean a nucleic acid which comprises coding sequences and regulatory sequences permitting the expression of said coding sequences, and in which the coding sequences are sequences which are not normally present in the genome of a parent virus employed in the present invention or, if they are present, are in a different genomic context. In the context of the invention, the exogenous DNA sequence [perhaps [sic]] composed of one or more genes. The regulatory sequences may be of any origin.

Page 12, Paragraph Beginning on Line 7

According to another embodiment, a method according to the invention may also be employed to insert at least two DNA fragments within the viral genome, by intermolecular recombination between (i) a first DNA fragment comprising all or part of said genome of the parent virus, (ii) a second DNA fragment comprising a first portion of said exogenous DNA sequence equipped at its 5' end with said flanking [sequences [sic]] sequence A and (iii) a third DNA fragment comprising a second portion of said exogenous DNA sequence

equipped at its 3' end with said flanking [sequences [sic]] sequence B; said second and third DNA fragments containing a homologous sequence overlapping at their respective 3' and 5' ends. As a guide, these sequences which are homologous between the second and third DNA fragments satisfy the same criteria of homology and of length as the sequences A and B. This specific embodiment is especially advantageous for the cloning of large-sized exogenous sequences.

Page 13, Paragraph Beginning on Line 38

The present invention also covers the use of an infectious viral particle or of a recombinant viral vector prepared according to a method according to the invention, for the therapeutic or surgical treatment of the human body, and in particular by gene therapy. A method according to the invention is intended more especially for the preventive or curative treatment of diseases such as genetic diseases (hemophilia; thalassemias, emphysema, Gaucher's disease, cystic fibrosis, [Duchène's [sic]] Duchenne's or Becker's myopathy, etc.), cancers and viral diseases (AIDS, herpes infections or infections caused by cytomegalovirus or by papillomavirus). For the purposes of the present invention, the vectors and viral particles prepared by a method according to the invention may be introduced either *in vitro* into a host cell removed from the patient, or directly *in vivo* into the body to be treated. Preferably, the host cell is a human cell, and preferably a lung, fibroblast, muscle, liver or lymphocytic cell or a cell of the hematopoietic line.

Page 18, Paragraph Beginning on Line 14

A cassette for the expression of a gene coding for the gp19 protein of the Ad5 E3 region (nucleotides 28731 to 29217) is assembled in the bacteriophage M13mp18 (Gibco BRL) by cloning two PCR fragments, one corresponding to the RSV (Rous sarcoma virus) 3' LTR (oligonucleotide primers oTG5892-SEQ ID NO: 4 and 5893-SEQ ID NO: 5) and the other to the sequence coding for gp19 (oTG5455-SEQ ID NO: 6 and 5456-SEQ ID NO: 7). The vector M13TG1683 is obtained, from which the expression cassette is excised by an *Xba*I digestion. After treatment with Klenow, it is introduced into the *Bsm*I site (blunted by the action of phage T4 DNA polymerase) of pTG8519. The latter is derived from the plasmid puc 19 [[sic]] (Gibco BRL), into which the adenoviral sequences lying between the *Spe*I site and the right-hand end of the genome (nucleotides 27082 to 35935) but lacking the majority of the E3 region (nucleotides 27871 to 30758) have been inserted. pTG1695 is obtained, the *Sca*I-*Spe*I fragment of which, carrying the plasmid sequences, is replaced by a purified equivalent fragment of pTG1659. The latter corresponds to puc 19 [[sic]] comprising the Ad5 sequences extending from nucleotides 21562 to 35826. pTG1697 thereby obtained possesses adenoviral sequences which extend from the *Bam*HI (position 21562) site to the 3' ITR (position 35935), in which sequences the E3 region is replaced by a gp19 expression cassette under the control of the RSV constitutive promoter. The *Dra*I fragment (position 22444 and 35142 on the Ad5 genome) is purified, and cointroduced into competent BJ-5183 bacteria with pTG3602 linearized with *Spe*I and treated with Klenow. The recombinants carrying a plasmid generated by recombination are screened for the presence of the RSV promoter. pTG3605, a plasmid vector carrying the Ad-gp19+ genome, is thus demonstrated.

Page 19, Paragraph Beginning on Line 9

The infectious power [[lacuna]] viral genome excised from plasmid pTG3605 is tested according to the protocol already described above. The production of a functional gp19 protein is monitored by co-immunoprecipitation of the antigens of the major histocompatibility complex class I and of the protein (Burgert and Kvist, 1985, Cell, *41*, 987-997).--

Page 23, Paragraph Beginning on Line 32

CAV2 virus (strain Toronto A 26/61; ATCC VR-800) genomic DNA is prepared by the standard technique (amplification on a dog kidney line MDCK GHK, etc., lysis of the cells, purification of the viruses by centrifugation on cesium chloride, treatment with proteinase k [[sic]] and lastly phenol/chloroform extraction). The CAV2 genome, which is 31 kbp in length, is introduced into a plasmid vector by homologous recombination. For this purpose, the left-hand and right-hand ends of the CAV2 genome are isolated by PCR and enzymatic digestion, incorporating a *Not*I site immediately beyond the 5' and 3' ITRs. The vector pTG4457 is obtained by introducing into p polyII the 5' portion of the viral genome as far as the *Bst*BI site (position 870) followed by the 3' portion starting from the *Sal*I site (position 27800). The complete genome may be reconstituted by cotransformation between the genomic DNA (100 to 500 ng) and pTG4457 digested with *Bst*BI (10 to 100 ng). The viral genome may be excised from the above vector pTG5406 by *Not*I digestion. It is vertified that the DNA is infectious by transfection of 1 to 5 μg into dog MDCK or GHK cells. The production of plaques is observed.--